L5 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:639164 CAPLUS Full-text
DN 149:17704
TI Stable parenteral formulation containing a benzodiazepine antiviral agent
IN Buranachokpaisan, Thitiwan; Jiang, Wenlei; Tong, Wei-Qin
PA Novartis A.-G., Switz.
SO PCT Int. Appl., 18pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

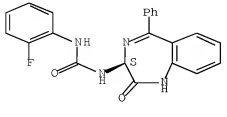
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2008063634	A1	20080529	WO 2007-US24246	20071120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2006-866646P	P	20061121		

AB The present invention relates to pharmaceutical formulations of benzodiazepine compds. which are active against respiratory syncytial virus (RSV), suitable for parenteral administration for treatment of a RSV infection in pediatric patients. Thus, 6 mg/mL (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H- benzo[e][1,4]diazepin-3-yl)urea (free base equivalent) was dissolved in 40% hydroxypropyl β-cyclodextrin (HPβCD), with addition of 15 mM phosphate buffer, pH 7. The lyophilized cake of this solution was reconstituted with 3.8 mL of 5% dextrose solution to obtain 4.4 mL of 3 mg/mL (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H- benzo[e][1,4]diazepin-3-yl)urea in 20% HPβCD.

IT 676128-63-5, (S)-1-(2-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 959391-58-3
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of stable parenteral formulation of benzodiazepine antiviral agent containing cyclodextrin for treatment of pediatric respiratory syncytial virus infections)

RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

Absolute stereochemistry.

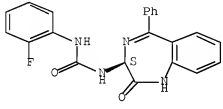


RN 959391-58-3 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)-, benzenesulfonate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 676128-63-5
CMF C22 H17 F N4 O2

Absolute stereochemistry.



CM 2

CRN 98-11-3
CMF C6 H6 O3 S

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:352859 CAPLUS Full-text
DN 148:394354
TI Compositions and methods for treatment of viral diseases
IN Johansen, Lisa M.; Owens, Christopher M.; Mawhinney, Christina; Chappell, Todd W.; Brown, Alexander T.; Frank, Michael G.; Altmeyer, Ralf
PA Combinatorx (Singapore) Pre. Ltd., Singapore
SO PCT Int. Appl., 237pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

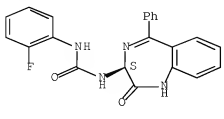
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2008033466	A2	20080320	WO 2007-US19932	20070913
	WO 2008033466	A3	20081211		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
	US 20080161324	A1	20080703	US 2007-900893	20070913
PRAI	US 2006-844463P	P	20060914		
	US 2006-874061P	P	20061211		

AB Based on the results of the authors screen identifying compds. and combinations of compds. having antiviral activity, the present invention features compns., methods, and kits useful in the treatment of viral diseases. In certain embodiments, the viral disease is caused by a single stranded RNA virus, a flaviviridae virus, or a hepatic virus. In particular embodiments, the viral disease is viral hepatitis (e.g., hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E). Also featured are screening methods for identification of novel compds. that may be used to treat a viral disease.

IT 676128-63-5, RSV 604
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. and methods for treatment of viral diseases)

RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

Absolute stereochemistry.

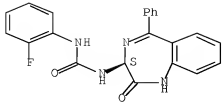


L5 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:1396512 CAPLUS Full-text
DN 148:39892
TI Salts and crystal modifications of 1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea
IN Feng, Lili; Jiang, Xinglong; Karpinski, Piotr
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 21pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

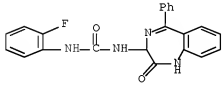
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007140154	A2	20071206	WO 2007-US69327	20070521
	WO 2007140154	A3	20080320		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
	AU 2007267671	A1	20071206	AU 2007-267671	20070521
	CA 2650514	A1	20071206	CA 2007-2650514	20070521
	EP 2029556	A2	20090304	EP 2007-797606	20070521
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				
	KR 2009009898	A	20090123	KR 2008-728592	20081121
	NO 2008005000	A	20081223	NO 2008-5000	20081128
PRAI	US 2006-802836P	P	20060523		
	WO 2007-US69327	W	20070521		

AB The invention relates to salts of 1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea and crystalline forms thereof, their production and usage, and pharmaceutical prepns. containing such salts and crystalline forms. Thus, to 50 mg of RSV604 free base dissolved in 2 mL of acetone (or acetonitrile) were added 40 mg of benzenesulfonic acid resulting in precipitation Then, 2 to 4 mL of tert-Bu Me ether antisolvent was added, and solid was filtered and dried to give RSV604 besylate monohydrate salt.
IT 676128-63-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(RSV 604; preparation of salts and crystal modifications of 1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea for dosage forms for infection treatment)
RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

Absolute stereochemistry.



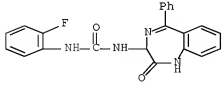
IT 676128-62-4DP, 1-(2-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, salts 959391-56-1P 959391-57-2P 959391-58-3P 959391-59-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of salts and crystal modifications of 1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea for dosage forms for infection treatment)
RN 676128-62-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)- (CA INDEX NAME)



RN 959391-56-1 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)-, benzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 676128-62-4
CMF C22 H17 F N4 O2



CM 2

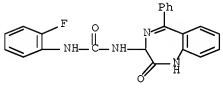
CRN 98-11-3

CMF C6 H6 O3 S

RN 959391-57-2 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)-, benzenesulfonate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 676128-62-4
CMF C22 H17 F N4 O2



CM 2

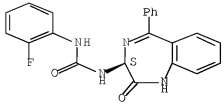
CRN 98-11-3
CMF C6 H6 O3 S

RN 959391-58-3 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)-, benzenesulfonate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 676128-63-5
CMF C22 H17 F N4 O2

Absolute stereochemistry.



CM 2

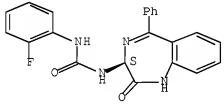
CRN 98-11-3
CMF C6 H6 O3 S

RN 959391-59-4 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)-, benzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 676128-63-5
CMF C22 H17 F N4 O2

Absolute stereochemistry.



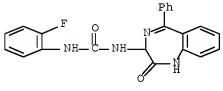
CM 2

CRN 98-11-3
CMF C6 H6 O3 S

IT 676128-62-4, 1-(2-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of salts and crystal modifications of 1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea for dosage forms for infection treatment)

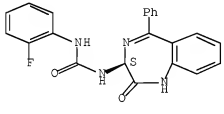
RN 676128-62-4 CAPLUS

CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)- (CA INDEX NAME)



L5 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:1021168 CAPLUS Full-text
DN 147:461629
TI RSV604, a novel inhibitor of respiratory syncytial virus replication
AU Chapman, Joanna; Abbott, Elizabeth; Alber, Dagmar G.; Baxter, Robert C.; Bithell, Sian K.; Henderson, Elisa A.; Carter, Malcolm C.; Chambers, Phil; Chubb, Ann; Cockerill, G. Stuart; Collins, Peter L.; Dowdell, Verity C. L.; Keegan, Sally J.; Kelsey, Richard D.; Lockyer, Michael J.; Luongo, Cindy; Najarro, Pilar; Pickles, Raymond J.; Simmonds, Mark; Taylor, Debbie; Tyms, Stan; Wilson, Lara J.; Powell, Kenneth L.
CS Arrow Therapeutics Ltd., London, SE1 1DB, UK
SO Antimicrobial Agents and Chemotherapy (2007), 51(9), 3346-3353
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infections worldwide, yet no effective vaccine or antiviral treatment is available. Here we report the discovery and initial development of RSV604, a novel benzodiazepine with submicromolar anti-RSV activity. It proved to be equipotent against all clin. isolates tested of both the A and B subtypes of the virus. The compound has a low rate of in vitro resistance development. Sequencing revealed that the resistant virus had mutations within the nucleocapsid protein. This is a novel mechanism of action for anti-RSV compds. In a three-dimensional human airway epithelial cell model, RSV604 was able to pass from the basolateral side of the epithelium effectively to inhibit virus replication after mucosal inoculation. RSV604, which is currently in phase II clin. trials, represents the first in a new class of RSV inhibitors and may have significant potential for the effective treatment of RSV disease.
IT 676128-63-5, RSV 604
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RSV604 as inhibitor of respiratory syncytial virus replication)
RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

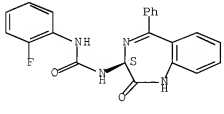
Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

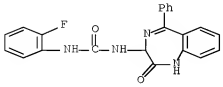
L5 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:253120 CAPLUS Full-text
DN 146:371914
TI 1,4-Benzodiazepines as Inhibitors of Respiratory Syncytial Virus. The Identification of a Clinical Candidate
AU Henderson, Elisa A.; Alber, Dagmar G.; Baxter, Robert C.; Bithell, Sian K.; Budworth, Joanna; Carter, Malcolm C.; Chubb, Ann; Cockerill, G. Stuart; Dowdell, Verity C. L.; Fraser, Ian J.; Harris, Robert A.; Keegan, Sally J.; Kelsey, Richard D.; Lumley, James A.; Stables, Jeremy N.; Weerasekera, Natasha; Wilson, Lara J.; Powell, Kenneth L.
CS Arrow Therapeutics, Britannia House, London, SE1 1DA, UK
SO Journal of Medicinal Chemistry (2007), 50(7), 1685-1692
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 146:371914
AB Respiratory syncytial virus (RSV) is the cause of one-fifth of all lower respiratory tract infections worldwide and is increasingly being recognized as representing a serious threat to patient groups with poorly functioning or immature immune systems. Racemic 1,4-benzodiazepines show potent anti-RSV activity in vitro. Anti-RSV evaluation of 3-position R- and S-benzodiazepine enantiomers and subsequent optimization of this series resulted in selection of a clin. candidate. Antiviral activity was found to reside mainly in the S-enantiomer, and the R-enantiomers were consistently less active against RSV. Analogs of 1,4-(S)-benzodiazepine were synthesized as part of the lead optimization program at Arrow and tested in the XTT assay. From this exercise, (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]- diazepin-3-yl)-urea, 17b (RSV-604) was identified as a clin. candidate, exhibiting potent anti-RSV activity in the XTT assay, which was confirmed in secondary assays. Compound 17b also possessed a good pharmacokinetic profile and has now progressed into the clinic.
IT 676128-63-5P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzodiazepines as inhibitors of respiratory syncytial virus)
RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

Absolute stereochemistry.



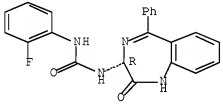
IT 676128-62-4P 932108-20-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzodiazepines as inhibitors of respiratory syncytial virus)

RN 676128-62-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)- (CA INDEX NAME)



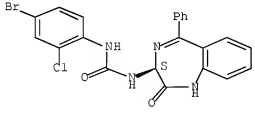
RN 932108-20-8 CAPLUS
CN Urea, N-[(3R)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

Absolute stereochemistry.



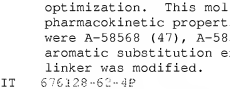
IT 932108-23-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(benzodiazepines as inhibitors of respiratory syncytial virus)
RN 932108-23-1 CAPLUS
CN Urea, N-(4-bromo-2-chlorophenyl)-N'-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)

Absolute stereochemistry.

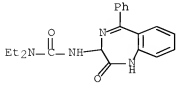


RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:208362 CAPLUS Full-text
DN 144:444888
TI 1,4-Benzodiazepines as Inhibitors of Respiratory Syncytial Virus
AU Carter, Malcolm C.; Alber, Dagmar G.; Baxter, Robert C.; Bithell, Sian K.; Budworth, Jo; Chubb, Ann; Cockerill, G. Stuart; Dowdell, Verity C. L.; Henderson, Elisa A.; Keegan, Sally J.; Kelsey, Richard D.; Lockyer, Michael J.; Stables, Jeremy N.; Wilson, Lara J.; Powell, Kenneth L.
CS Arrow Therapeutics Ltd, London, SE1 1DA, UK
SO Journal of Medicinal Chemistry (2006), 49(7), 2311-2319
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 144:444888
AB Respiratory syncytial virus (RSV) is the cause of one-fifth of all lower respiratory tract infections worldwide and is increasingly being recognized as a serious threat to patient groups with poorly functioning immune systems. Our approach to finding a novel inhibitor of this virus was to screen a 20 000-member diverse library in a whole cell XTT assay. Parallel assays were carried out in the absence of virus in order to quantify any associated cell toxicity. This identified 100 compds. with IC50's less than 50 μM. A-33903 (18), a 1,4-benzodiazepine analog, was chosen as the starting point for lead optimization. This mol. was moderately active and demonstrated good pharmacokinetic properties. The most potent compds. identified from this work were A-58568 (47), A-58569 (44), and A-62066 (46), where modifications to the aromatic substitution enhanced potency, and A-58175 (42), where the amide linker was modified.
IT 676128-62-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(1,4-Benzodiazepines as Inhibitors of Respiratory Syncytial Virus)
RN 676128-62-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)- (CA INDEX NAME)



IT 676127-95-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(1,4-Benzodiazepines as Inhibitors of Respiratory Syncytial Virus)
RN 676127-95-0 CAPLUS
CN Urea, N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N,N-diethyl- (CA INDEX NAME)

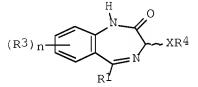


RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1042227 CAPLUS Full-text
DN 143:326401
TI Process for preparing benzodiazepines
IN Dowdell, Verity; Kelsey, Richard David; Carter, Malcolm; Henderson, Elisa Ann
PA Arrow Therapeutics Limited, UK
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005090319	A1	20050929	WO 2005-GB1050	20050321
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 20070293482	A1	20071220	US 2007-593665	20070802
PRAI	GB 2004-6280	A	20040319		
	GB 2004-6282	A	20040319		
	GB 2004-23462	A	20041021		
	WO 2005-GB1050	W	20050321		

OS CASREACT 143:326401; MARPAT 143:326401
GI



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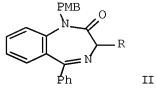
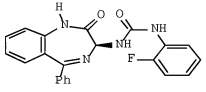


II



III

AB A process for the preparation of benzodiazepines (R/S)-I [wherein R1 = alkyl or (hetero)aryl; R3 = halo, OH, alkyl; n = 0-3; X = -NH-, -N(alkyl)-, -CO-; R4 = H, CONH(alkyl); etc., or pharmaceutically acceptable salts thereof], which are active against respiratory syncytial virus (RSV), is disclosed. Some intermediates are claimed. As an example, acylation of 2-aminoacetophenone with bromoacetyl bromide (95%) followed by cyclocondensation with NH3 in refluxing methanol (95%) and subsequent N-protection with PMB-Cl (87%) gave benzodiazepine II (R = H). This compound underwent oximation with isoamyl nitrite in the presence of KOBu-t in toluene to afford oxime II (R = =NOH) (76%), which was reduced with H2-Ru/C to amine II (R = NH2) (81%). Crystallization induced dynamic resolution of the above racemate amine with (-)-Boc-Phe-OH (1 equivalent) and 3,5-dichlorosalicylaldehyde (0.04 equivalent) in toluene under stirring at rt provided (S)-II (R = NH2) (71% yield, 99.8%

e.e.). Following condensation with 2-fluorophenylisocyanate and deprotection with AlCl3 in anisole led to urea III (91% for two steps).

IT 119506-63-3P, 1-(3-Methoxyphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 206115-22-3P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(m-tolyl)urea 676127-95-0P, 1,1-Diethyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-54-4P, 1-(2-Methoxyphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-55-5P, 1-(2-Nitrophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-57-7P, 1-(2-Chlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-59-9P, 1-(4-Chlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-61-3P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(p-tolyl)urea 676128-62-4P, 1-(2-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-63-5P 676128-64-6P, 1-(4-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-81-7P, 1-(2-Fluorobenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-82-8P, 1-(4-Methoxybenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-83-9P, 1-(3-Methylbenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-84-0P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-trifluoromethylphenyl)urea 676129-10-5P, 1-(3,5-Dimethylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-11-6P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-trifluoromethoxyphenyl)urea 676129-12-7P, 1-(4-Bromo-2-trifluoromethylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-13-8P, 1-(4-Bromobenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-14-9P, 1-(2,3-Dichlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-15-0P, 1-(2,6-Dimethylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-16-1P, 1-(2-Chloro-6-methylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-17-2P, 1-(4-Nitrophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-18-3P, 1-(2-Methylsulfanylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-19-4P , 1-(2,6-Dichlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-22-9P, 1-(2,6-Difluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-23-0P, 1-(3-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-25-2P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(3-trifluoromethylphenyl)urea 676129-27-4P, 1-(3-Chlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-42-3P, 3-(2-Fluorophenyl)-1-methyl-1-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-44-5P, 1-tert-Butyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-45-6P, 1-Cyclohexyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-46-7P, 1-Ethyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-47-8P, 1-Butyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-65-0P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(thiophen-2-yl)urea 676129-66-1P,

1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(thiophen-3-yl)urea 865471-65-4P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxyphenyl)urea
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of 3-aminobenzodiazepines via oxidation of benzodiazepines with isoamyl nitrite followed by Ru/C-catalyzed hydrogenation and crystallization induced dynamic resolution)

RN 119506-69-3 CAPLUS
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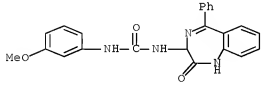

RN 206115-23-3 CAPLUS
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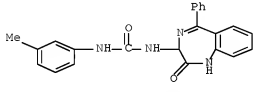
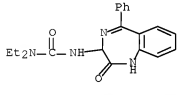


RN 676127-95-0 CAPLUS
CN Urea, N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N,N-diethyl- (CA INDEX NAME)



RN 676128-54-4 CAPLUS
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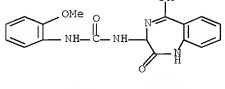

RN 676128-55-5 CAPLUS
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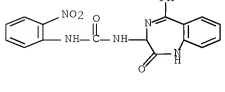
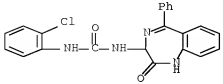


RN 676128-57-7 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



RN 676128-59-9 CAPLUS
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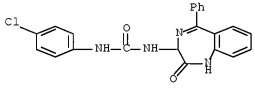

RN 676128-61-3 CAPLUS
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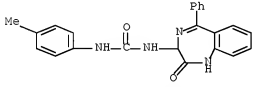

RN 676128-62-4 CAPLUS
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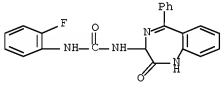
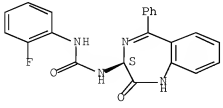
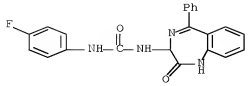


RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 676128-64-6 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-fluorophenyl)- (CA INDEX NAME)



RN 676128-81-7 CAPLUS
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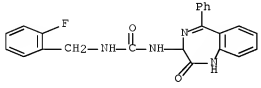

RN 676128-82-8 CAPLUS
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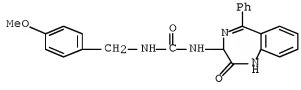

RN 676128-83-9 CAPLUS
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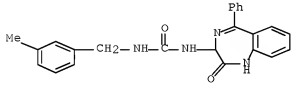

RN 676128-84-0 CAPLUS
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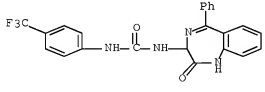

RN 676129-10-5 CAPLUS
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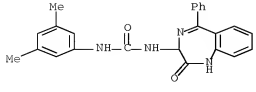

RN 676129-11-6 CAPLUS
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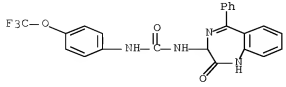
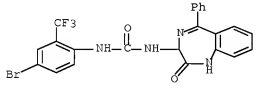
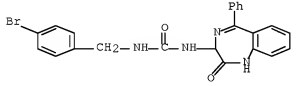


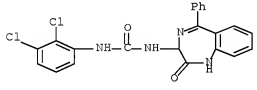
RN 676129-12-7 CAPLUS
CN Urea, N-[4-bromo-2-(trifluoromethyl)phenyl]-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



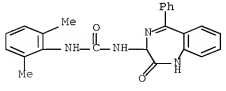
RN 676129-13-8 CAPLUS
CN Urea, N-[(4-bromophenyl)methyl]-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



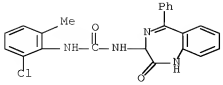
RN 676129-14-9 CAPLUS
CN Urea, N-(2,3-dichlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



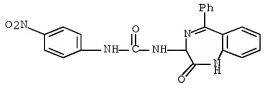
RN 676129-15-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2,6-dimethylphenyl)- (CA INDEX NAME)



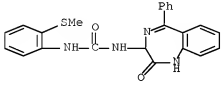
RN 676129-16-1 CAPLUS
CN Urea, N-(2-chloro-6-methylphenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



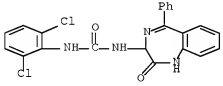
RN 676129-17-2 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-nitrophenyl)- (CA INDEX NAME)



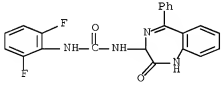
RN 676129-18-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[2-(methylthio)phenyl]- (CA INDEX NAME)



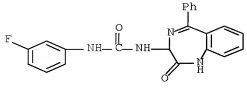
RN 676129-19-4 CAPLUS
CN Urea, N-(2,6-dichlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



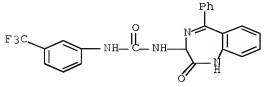
RN 676129-22-9 CAPLUS
CN Urea, N-(2,6-difluorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



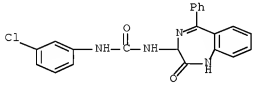
RN 676129-23-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-fluorophenyl)- (CA INDEX NAME)



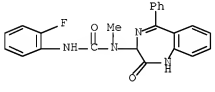
RN 676129-25-2 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



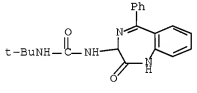
RN 676129-27-4 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



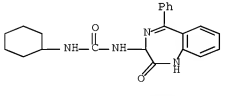
RN 676129-42-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)-N-methyl- (CA INDEX NAME)



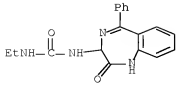
RN 676129-44-5 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(1,1-dimethylethyl)- (CA INDEX NAME)



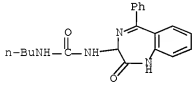
RN 676129-45-6 CAPLUS
CN Urea, N-cyclohexyl-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



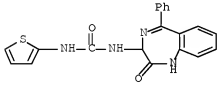
RN 676129-46-7 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-ethyl- (CA INDEX NAME)



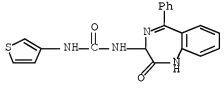
RN 676129-47-8 CAPLUS
CN Urea, N-butyl-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-
(CA INDEX NAME)



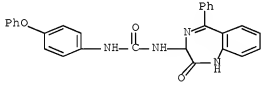
RN 676129-65-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-2-
thienyl- (CA INDEX NAME)



RN 676129-66-1 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-3-
thienyl- (CA INDEX NAME)



RN 865471-65-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-
phenoxyphenyl)- (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1042075 CAPLUS Full-text
DN 143:347207
TI Preparation of RSV replication-inhibiting benzodiazepine derivatives for use in pharmaceutical compositions in combination with RSV fusion protein inhibitors
IN Powell, Kenneth; Kelsey, Richard; Carter, Malcolm; Dowdell, Verity; Alber, Dagmar; Henderson, Elisa
PA Arrow Therapeutics Limited, UK
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005089771	A1	20050929	WO 2005-GB1029	20050318
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005224159	A1	20050929	AU 2005-224159	20050318
	CA 2557931	A1	20050929	CA 2005-2557931	20050318
	EP 1727551	A1	20061206	EP 2005-728747	20050318
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	CN 1933841	A	20070321	CN 2005-80008920	20050318
	BR 2005007652	A	20070710	BR 2005-7652	20050318
	JP 2007529491	T	20071025	JP 2007-503412	20050318
	MX 2006010709	A	20061116	MX 2006-10709	20060919
	IN 2006CN03411	A	20070706	IN 2006-CN3411	20060919
	KR 2007009630	A	20070118	KR 2006-721651	20061018
	US 20070185096	A1	20070809	US 2007-593382	20070314
PRAI	GB 2004-6279	A	20040319		
	WO 2005-GB1029	W	20050318		

OS CASREACT 143:347207; MARPAT 143:347207
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

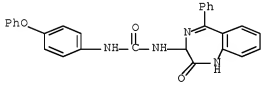
AB The invention is related to a pharmaceutical composition comprising pharmaceutically acceptable carrier or diluent and: (a) an inhibitor of the respiratory syncytial virus (RSV) fusion protein of formula I [X = H, (un)substituted alkyl; Y = hetero/aryl, alkyl, alkoxy, etc.; Z = CH2 and derivs.; R1 = H, CONH2 and derivs., CO2H and derivs., (un)substituted alkyl; R2 = H, NH2, alkenyl, etc.; R3 = H, alkenyl, CO2H, etc.; Q = 1,2-dihydrobenzotriazol-1-yl, 2,3-dihydroindazol-1-yl, etc.]; and (b) a benzodiazepine derivative of formula II [R1 = alkyl, hetero/aryl; R2 = H, alkyl; each R3 = independently halo, OH, alkyl, alkoxy, NH2, CN, etc.; n = 0-3; R4 = H, alkyl; X = CO, SO, SO2, CONH and derivs.; R5 = (un)substituted

hetero/aryl, heterocyclyl] capable of inhibiting RSV replication; the composition provides an additive and synergistic therapeutic effect in treating or preventing an RSV infection. The invention is also related to the preparation of benzodiazepines II. Thus, reacting (S)-3-Amino-5-phenyl-1,3-dihydrobenzo[e][1,4]diazepin-2-one with 2-chloro-4-(morpholin-4-yl)benzoic acid gave (S)-III. The fractional inhibitory concentration (FIC) for benzodiazepine III in combination with benzimidazole IV = 0.3, demonstrating a synergistic interaction.

IT 865471-65-4P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxyphenyl)urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of RSV replication-inhibiting benzodiazepine derivs. for use in pharmaceutical compns. in combination with RSV fusion protein inhibitors)

RN 865471-65-4 CAPLUS

CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-phenoxyphenyl)- (CA INDEX NAME)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1042074 CAPLUS Full-text
DN 143:326400
TI Benzodiazepinones for treating or preventing human respiratory syncytial viral infection and other diseases
IN Dowdell, Verity; Carter, Malcolm; Alber, Dagmar; Henderson, Elisa
PA Arrow Therapeutics Limited, UK; Kelsey, Richard
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005089770	A1	20050929	WO 2005-GB1023	20050318
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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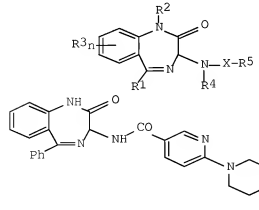
	CA 2557929	A1	20050929	CA 2005-2557929	20050318
	EP 1740185	A1	20070110	EP 2005-718065	20050318
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1929848	A	20070314	CN 2005-80008070	20050318
	BR 2005008968	A	20070821	BR 2005-8968	20050318
	JP 2007529490	T	20071025	JP 2007-503411	20050318
	MX 2006010710	A	20070308	MX 2006-10710	20060919
	IN 2006CN03425	A	20070706	IN 2006-CN3425	20060919
	KR 2007017357	A	20070209	KR 2006-721652	20061018
	US 20080139536	A1	20080612	US 2007-593667	20070802
PRAI	GB 2004-6280	A	20040319		
	WO 2005-GB1023	W	20050318		

OS CASREACT 143:326400; MARPAT 143:326400
GI



I

II

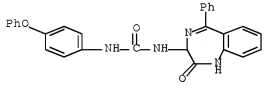
AB Use is claimed of benzodiazepinones (shown as I; variables defined below; e.g. 6-(4-methylpiperazin-1-yl)-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)nicotinamide (shown as II)) or an N-oxide thereof

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treating or preventing an human respiratory syncytial viral (RSV) infection. RSV antiviral activities for 52 examples of I are tabulated. For I: R1 = C1-6 alkyl, aryl or heteroaryl; R2 = H or C1-6 alkyl; each R3 = halogen, hydroxy, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C1-6 haloalkyl, C1-6 haloalkoxy, amino, mono(C1-6 alkyl)amino, di(C1-6alkyl)amino, nitro, cyano, CO2R', CONR'R'', NHCOR', S(O)R', S(O)2R', NHS(O)2R', S(O)NR'R'' or S(O)2NR'R'', wherein each R' and R'' = H or C1-6 alkyl; n = O to 3; R4 = H or C1-6 alkyl. X = CO, CONR', S(O) or S(O)2, wherein R' is H or a C1-C6 alkyl group; and R5 = a heteroaryl or heterocyclyl group which is substituted by a C1-C6 hydroxyalkyl group or a -(C1-C4 alkyl)-X1-(C1-C4 alkyl)-X2-(C1-C4 alkyl) group, wherein X1 = -O-, -S- or -NR', wherein R' = H or a C1-C4 alkyl group and X2 = CO, SO or SO2, or R55 = -A1-Y-A2, wherein A1 is an aryl, heteroaryl, carbocyclyl or heterocyclyl group; Y = a direct bond or a C1-C4 alkylene, SO2, CO, -O-, -S- or -NR' moiety, wherein R' is a C1-C6 alkyl group; and A2 is an aryl, heteroaryl, carbocyclyl or heterocyclyl group. Although the methods of preparation are not claimed, .apprx.50 example prepns. are included. For example, II was prepared in MeCN using microwave heating and Et3N from N-methylpiperazine and 6-chloro-N-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)nicotinamide, which was prepared in DMF from 3-amino-5-phenyl-1,3-dihydrobenzo[e][1,4]diazepin-2-one and 6-chloronicotinic acid using O-benzotriazol-1-yl-N,N,N',N'- tetramethyluronium hexafluorophosphate and Et3N.

IT 865471-65-4P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-phenoxyphenyl)urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; benzodiazepinones for treating or preventing human respiratory syncytial viral infection and other diseases)

RN 865471-65-4 CAPLUS

CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-phenoxyphenyl)- (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1042073 CAPLUS Full-text
DN 143:339599
TI Pharmaceutical composition comprising a benzodiazepine derivative and an inhibit or of the RSV fusion protein
IN Powell, Kenneth; Kelsey, Richard; Carter, Malcolm; Alber, Dagmar; Wilson, Lara; Henderson, Elisa; Chambers, Phil; Taylor, Debra; Tyms, Stan; Dowdell, Verity
PA Arrow Therapeutics Limited, UK
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005089769	A1	20050929	WO 2005-GB1018	20050318
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005224157	A1	20050929	AU 2005-224157	20050318
	CA 2558112	A1	20050929	CA 2005-2558112	20050318
	EP 1727550	A1	20061206	EP 2005-718061	20050318
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1933842	A	20070321	CN 2005-80008927	20050318
	BR 2005007654	A	20070710	BR 2005-7654	20050318
	JP 2007529489	T	20071025	JP 2007-503410	20050318
	MX 2006010711	A	20061116	MX 2006-10711	20060919
	IN 2006CN03430	A	20070706	IN 2006-CN3430	20060919
	KR 2007009629	A	20070118	KR 2006-721650	20061018
	US 20070142403	A1	20070621	US 2007-593666	20070312
PRAI	GB 2004-6282	A	20040319		
	WO 2005-GB1018	W	20050318		

OS MARPAT 143:339599
AB A pharmaceutical composition which comprises a pharmaceutically acceptable carrier or diluent and: (a) an inhibitor of the RSV fusion protein; and (b) a benzodiazepine derivative capable of inhibiting RSV replication is highly active against RSV.
IT 119506-69-3, 1-(3-Methoxyphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 206115-23-3, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-m-tolylurea 676128-54-4, 1-(2-Methoxyphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-55-5, 1-(2-Nitrophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-57-7, 1-(2-Chlorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-59-9, 1-(4-Chlorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-61-3, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-p-tolylurea 676128-62-4, 1-(2-Fluorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-63-5 676128-64-6,

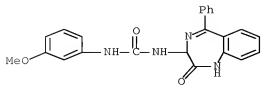
1-(4-Fluorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-81-7, 1-(2-Fluorobenzyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-82-8, 1-(4-Methoxybenzyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-83-9, 1-(3-Methylbenzyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676128-84-0, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-(4-trifluoromethylphenyl)urea 676129-10-5, 1-(3,5-Dimethylphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-11-6, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-(4-trifluoromethoxyphenyl)urea 676129-12-7, 1-(4-Bromo-2-trifluoromethylphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-13-8, 1-(4-Bromobenzyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-14-9, 1-(2,3-Dichlorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-15-0, 1-(2,6-Dimethylphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-16-1, 1-(2-Chloro-6-methylphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-17-2, 1-(4-Nitrophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-18-3, 1-(2-Methylsulfanylphenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-19-4, 1-(2,6-Dichlorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-22-9, 1-(2,6-Difluorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-23-0, 1-(3-Fluorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-25-2, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-(3-trifluoromethylphenyl)urea 676129-27-4, 1-(3-Chlorophenyl)-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-42-3, 3-(2-Fluorophenyl)-1-methyl-1-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-44-5, 1-tert-Butyl-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-45-6, 1-Cyclohexyl-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-46-7, 1-Ethyl-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-47-8, 1-Butyl-3-[2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]urea 676129-65-0, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-thiophen-2-ylurea 676129-66-1, 1-[2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl]-3-thiophen-3-ylurea

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

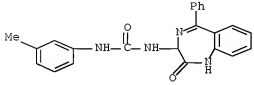
(antiviral benzodiazepine derivative as inhibitors of RSV fusion protein)

RN 119506-69-3 CAPLUS

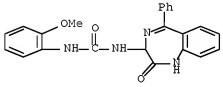
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-methoxyphenyl)- (CA INDEX NAME)



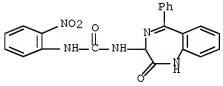
RN 206115-23-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-methylphenyl)- (CA INDEX NAME)



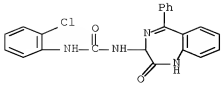
RN 676128-54-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-methoxyphenyl)- (CA INDEX NAME)



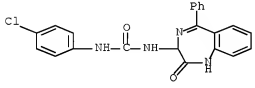
RN 676128-55-5 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-nitrophenyl)- (CA INDEX NAME)



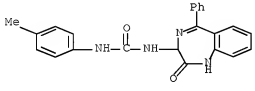
RN 676128-57-7 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



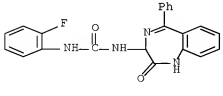
RN 676128-59-9 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



RN 676128-61-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-methylphenyl)- (CA INDEX NAME)

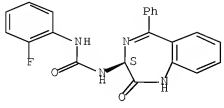


RN 676128-62-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)- (CA INDEX NAME)

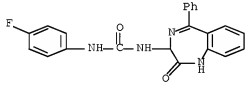


RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

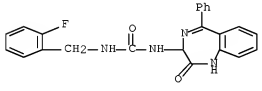
Absolute stereochemistry.



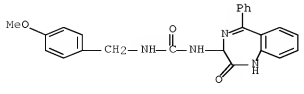
RN 676128-64-6 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-fluorophenyl)- (CA INDEX NAME)



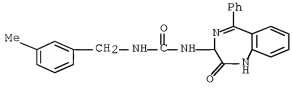
RN 676128-81-7 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[(2-fluorophenyl)methyl]- (CA INDEX NAME)



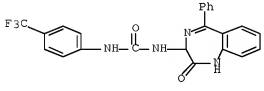
RN 676128-82-8 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[(4-methoxyphenyl)methyl]- (CA INDEX NAME)



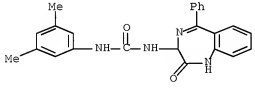
RN 676128-83-9 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[(3-methylphenyl)methyl]- (CA INDEX NAME)



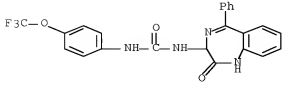
RN 676128-84-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



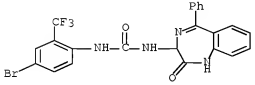
RN 676129-10-5 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3,5-dimethylphenyl)- (CA INDEX NAME)



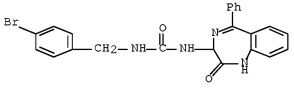
RN 676129-11-6 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[4-(trifluoromethoxy)phenyl]- (CA INDEX NAME)



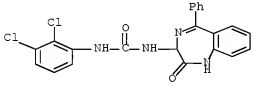
RN 676129-12-7 CAPLUS
CN Urea, N-[4-bromo-2-(trifluoromethyl)phenyl]-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



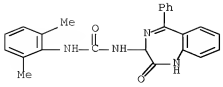
RN 676129-13-8 CAPLUS
CN Urea, N-[(4-bromophenyl)methyl]-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



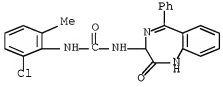
RN 676129-14-9 CAPLUS
CN Urea, N-(2,3-dichlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



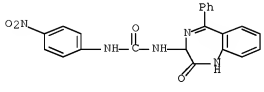
RN 676129-15-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2,6-dimethylphenyl)- (CA INDEX NAME)



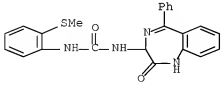
RN 676129-16-1 CAPLUS
CN Urea, N-(2-chloro-6-methylphenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



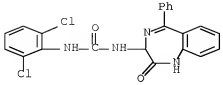
RN 676129-17-2 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-nitrophenyl)- (CA INDEX NAME)



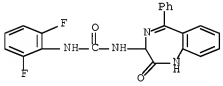
RN 676129-18-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[2-(methylthio)phenyl]- (CA INDEX NAME)



RN 676129-19-4 CAPLUS
CN Urea, N-(2,6-dichlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



RN 676129-22-9 CAPLUS
CN Urea, N-(2,6-difluorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



RN 676129-23-0 CAPLUS
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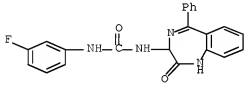

RN 676129-25-2 CAPLUS
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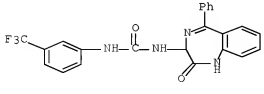
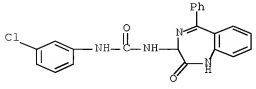
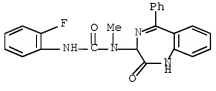


RN 676129-27-4 CAPLUS

CN Urea, N-(3-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



RN 676129-42-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)-N-methyl- (CA INDEX NAME)



RN 676129-44-5 CAPLUS
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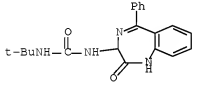

RN 676129-45-6 CAPLUS
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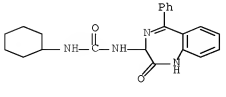

RN 676129-46-7 CAPLUS
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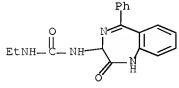
(CA INDEX NAME)



RN 676129-47-8 CAPLUS
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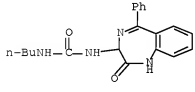
(CA INDEX NAME)



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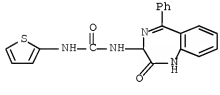

RN 676129-66-1 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-3-
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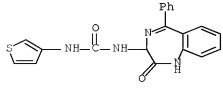

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:267311 CAPLUS Full-text
DN 140:287417
TI Preparation of aminobenzodiazepinones and pharmaceutical compositions containing them for use against respiratory syncytial virus
IN Carter, Malcolm; Henderson, Elisa; Kelsey, Richard; Wilson, Lara; Chambers, Phil; Taylor, Debra; Tyms, Stan
PA Arrow Therapeutics Limited, UK
SO PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004026843	A1	20040401	WO 2003-GB4050	20030922
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	CA 2499322	A1	20040401	CA 2003-2499322	20030922
	AU 2003267587	A1	20040408	AU 2003-267587	20030922
	EP 1539716	A1	20050615	EP 2003-748279	20030922
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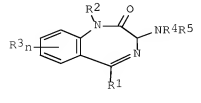
	BR 2003014595	A	20050809	BR 2003-14595	20030922
	CN 1694874	A	20051109	CN 2003-825190	20030922
	JP 2006503054	T	20060126	JP 2004-537305	20030922
	NZ 538870	A	20070427	NZ 2003-538870	20030922
	ZA 2005002001	A	20060628	ZA 2005-2001	20050309
	MX 2005002871	A	20051005	MX 2005-2871	20050315
	IN 2005CN00400	A	20070406	IN 2005-CN400	20050316
	NO 2005001908	A	20050419	NO 2005-1908	20050419
	US 20060040923	A1	20060223	US 2005-528250	20050621
	IN 2007CN04798	A	20080321	IN 2007-CN4798	20071026
PRAI	GB 2002-21923	A	20020920		
	GB 2003-2078	A	20030129		
	WO 2003-GB4050	W	20030922		
	IN 2005-CN400	A3	20050316		

OS MARPAT 140:287417
GI



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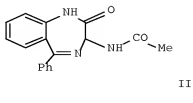


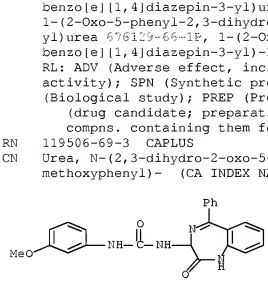
II

AB Benzodiazepines (shown as I; variables defined below; e.g. II) and pharmaceutically acceptable salts thereof, are active against respiratory syncytial virus (RSV). For I: R1 = C1-6 alkyl, aryl or heteroaryl; R2 = H or C1-6 alkyl; each R3 = halogen, hydroxy, C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C1-6 haloalkyl, C1-6 haloalkoxy, amino, mono(C1-6 alkyl)amino, di(C1-6 alkyl)amino, nitro, cyano, -CO2RI, -CONRIRII, -NH-CO-RI, -S(O)RI, -S(O)2RI, -NH-S(O)2RI, -S(O)NRIRII or -S(O)2NRIRII wherein each RI and RII = H or C1-6 alkyl; n = 0-3; R4 = H or C1-6 alkyl; R6 = C1-6 alkyl, aryl, heteroaryl, carbocyclyl, heterocyclyl, aryl-(C1-6 alkyl)-, heteroaryl-(C1-6 alkyl)-, carbocyclyl-(C1-6 alkyl)-, heterocyclyl-(C1-6 alkyl)-, aryl-C(O)-C(O)-, heteroaryl-C(O)-C(O)-, carbocyclyl-C(O)-C(O)-, heterocyclyl-C(O)-C(O)- or -XR6. X = -CO-, -S(O)- or -S(O)2-; and R6 = C1-6 alkyl, hydroxy, C1-6 alkoxy, C1-6 alkylthio, aryl, heteroaryl, carbocyclyl, heterocyclyl, aryl-(C1-6 alkyl)-, heteroaryl-(C1-6 alkyl)-, carbocyclyl-(C1-6 alkyl)-, heterocyclyl-(C1-6 alkyl)-, aryl-(C1-6hydroxyalkyl)-, heteroaryl-(C1-6 hydroxyalkyl)-, carbocyclyl-(C1-6 hydroxyalkyl)-, heterocyclyl-(C1-6 hydroxyalkyl)-, aryl-(C1-6alkyl)-O-, heteroaryl-(C1-6alkyl)-O-, carbocyclyl-(C1-6 alkyl)-O-, heterocyclyl-(C1-6 alkyl)-O- or -NRIRII wherein each RI and RII = H, C1-6 alkyl, carbocyclyl, heterocyclyl, aryl, heteroaryl, aryl-(C1-6 alkyl)-, heteroaryl-(C1-6 alkyl)-, carbocyclyl-(C1-6 alkyl)- or heterocyclyl-(C1-6 alkyl)-. Although the methods of preparation are not claimed, .apprx.80 example prepns. are included. For example, II was prepared by N-acetylation of 3-amino-5-phenyl-1,3- dihydrobenzo[e][1,4]diazepin-2-one; the reactant was prepared by deprotection of (2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3- yl)carbamic acid benzyl ester, which was prepared by cyclization of (2-aminophenyl)phenylmethanone with (benzotriazol-1-yl)(benzyloxycarbonylamino)acetic acid, which was prepared from glyoxylic acid monohydrate, benzotriazole and benzyl carbamate in toluene. Values for inhibition of RSV and toxicity were determined for >100 examples of I.

IT 119506-69-3P, 1-(3-Methoxyphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 206115-23-3P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(m-tolyl)urea 676128-57-7P, 1-(2-Chlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-59-9P, 1-(4-Chlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-61-3P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(p-tolyl)urea 676128-62-4P, 1-(2-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-63-5P, (S)-1-(2-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-64-6P, 1-(4-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-81-7P, 1-(2-Fluorobenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-82-8P, 1-(4-Methoxybenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-83-9P, 1-(3-Methylbenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676128-84-0P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-trifluoromethylphenyl)urea 676129-10-5P, 1-(3,5-Dimethylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-11-6P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(4-trifluoromethoxyphenyl)urea 676129-12-7P, 1-(4-Bromo-2-trifluoromethylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-13-8P, 1-(4-Bromobenzyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-14-9P, 1-(2,3-Dichlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-15-0P, 1-(2,6-Dimethylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-

benzo[e][1,4]diazepin-3-yl)urea 676129-16-1P, 1-(2-Chloro-6-methylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-17-2P, 1-(4-Nitrophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-18-3P, 1-(2-Methylsulfanylphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-19-4P, 1-(2,6-Dichlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-22-9P, 1-(2,6-Difluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-23-0P, 1-(3-Fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-25-2P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(3-trifluoromethylphenyl)urea 676129-27-4P, 1-(3-Chlorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-42-3P, 3-(2-Fluorophenyl)-1-methyl-1-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-44-5P, 1-tert-Butyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-45-6P, 1-Cyclohexyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-46-7P, 1-Ethyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-47-8P, 1-Butyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea 676129-65-0P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(thiophen-2-yl)urea 676129-66-1P, 1-(2-Oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)-3-(thiophen-3-yl)urea
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aminobenzodiazepinones and pharmaceutical compns. containing them for use against respiratory syncytial virus)

RN 119506-69-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-methoxyphenyl)- (CA INDEX NAME)



RN 206115-23-3 CAPLUS
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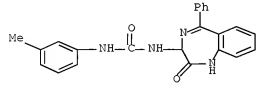
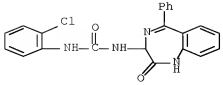
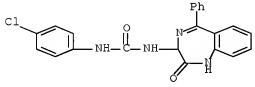


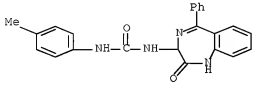
RN 676128-57-7 CAPLUS
CN Urea, N-(2-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



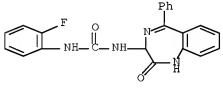
RN 676128-59-9 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



RN 676128-61-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-methylphenyl)- (CA INDEX NAME)

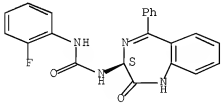


RN 676128-62-4 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)- (CA INDEX NAME)

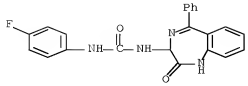


RN 676128-63-5 CAPLUS
CN Urea, N-[(3S)-2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl]-N'-(2-fluorophenyl)- (CA INDEX NAME)

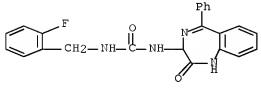
Absolute stereochemistry.



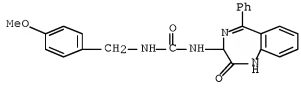
RN 676128-64-6 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-fluorophenyl)- (CA INDEX NAME)



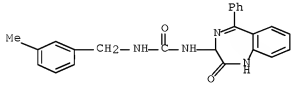
RN 676128-81-7 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[(2-fluorophenyl)methyl]- (CA INDEX NAME)



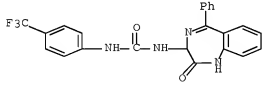
RN 676128-82-8 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[(4-methoxyphenyl)methyl]- (CA INDEX NAME)



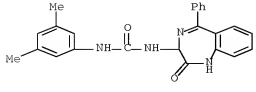
RN 676128-83-9 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[(3-methylphenyl)methyl]- (CA INDEX NAME)



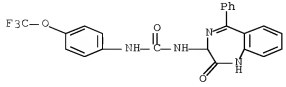
RN 676128-84-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[4-(trifluoromethyl)phenyl]- (CA INDEX NAME)



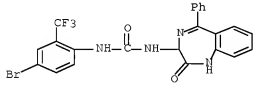
RN 676129-10-5 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3,5-dimethylphenyl)- (CA INDEX NAME)



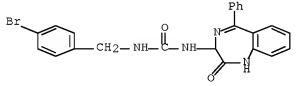
RN 676129-11-6 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[4-(trifluoromethoxy)phenyl]- (CA INDEX NAME)



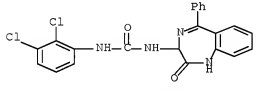
RN 676129-12-7 CAPLUS
CN Urea, N-[4-bromo-2-(trifluoromethyl)phenyl]-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



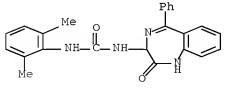
RN 676129-13-8 CAPLUS
CN Urea, N-[(4-bromophenyl)methyl]-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



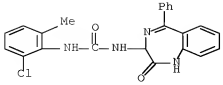
RN 676129-14-9 CAPLUS
CN Urea, N-(2,3-dichlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



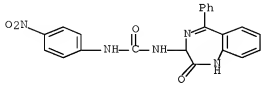
RN 676129-15-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2,6-dimethylphenyl)- (CA INDEX NAME)



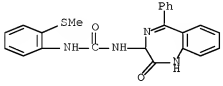
RN 676129-16-1 CAPLUS
CN Urea, N-(2-chloro-6-methylphenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



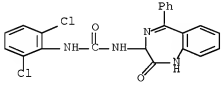
RN 676129-17-2 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(4-nitrophenyl)- (CA INDEX NAME)



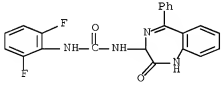
RN 676129-18-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[2-(methylthio)phenyl]- (CA INDEX NAME)



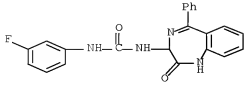
RN 676129-19-4 CAPLUS
CN Urea, N-(2,6-dichlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



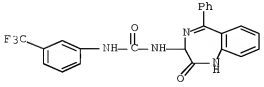
RN 676129-22-9 CAPLUS
CN Urea, N-(2,6-difluorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



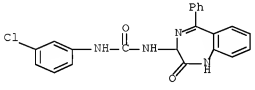
RN 676129-23-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-fluorophenyl)- (CA INDEX NAME)



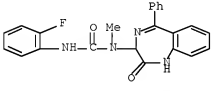
RN 676129-25-2 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)



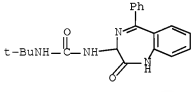
RN 676129-27-4 CAPLUS
CN Urea, N-(3-chlorophenyl)-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



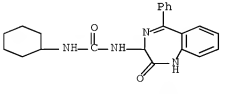
RN 676129-42-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-fluorophenyl)-N-methyl- (CA INDEX NAME)



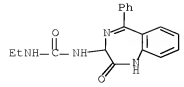
RN 676129-44-5 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(1,1-dimethylethyl)- (CA INDEX NAME)



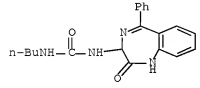
RN 676129-45-6 CAPLUS
CN Urea, N-cyclohexyl-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)- (CA INDEX NAME)



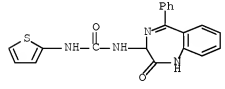
RN 676129-46-7 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-ethyl- (CA INDEX NAME)



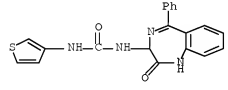
RN 676129-47-8 CAPLUS
CN Urea, N-butyl-N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-
(CA INDEX NAME)



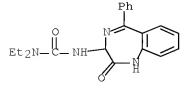
RN 676129-65-0 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-2-
thienyl- (CA INDEX NAME)



RN 676129-66-1 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-3-
thienyl- (CA INDEX NAME)

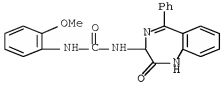


IT 676127-95-0P, 1,1-Diethyl-3-(2-oxo-5-phenyl-2,3-dihydro-1H-
benzo[e][1,4]diazepin-3-yl)urea 676128-54-4P,
1-(2-Methoxyphenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-
3-yl)urea 676128-55-5P, 1-(2-Nitrophenyl)-3-(2-oxo-5-phenyl-2,3-
dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(drug candidate; preparation of aminobenzodiazepinones and pharmaceutical
compns. containing them for use against respiratory syncytial virus)
RN 676127-95-0 CAPLUS
CN Urea, N'-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N,N-
diethyl- (CA INDEX NAME)

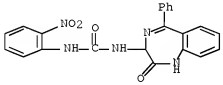


RN 676128-54-4 CAPLUS

CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-methoxyphenyl)- (CA INDEX NAME)

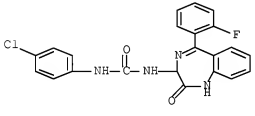


RN 676128-55-5 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(2-nitrophenyl)- (CA INDEX NAME)



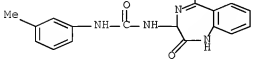
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1999:414228 CAPLUS Full-text
DN 131:193709
TI Quantitative structure-activity relationship study on some nonpeptidal cholecystokinin antagonists
AU Sinha, Jyoti; Kurup, Alka; Paleti, Anitha; Gupta, S. P.
CS Birla Institute of Technology and Science, Pilani, 333 031, India
SO Bioorganic & Medicinal Chemistry (1999), 7(6), 1127-1130
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB A quant. structure-activity relationship (QSAR) anal. has been performed on a series of 1,4-benzodiazepine derivs., which were found to act as antagonists of cholecystokinin (CCK), a gastrointestinal peptide hormone. The CCK acts with three different receptor subtypes termed as CCK-A, CCK-B, and gastrin receptor, which can be found in peripheral system, brain, and stomach, resp. With all the three subtypes, the binding of the compds. is found to significantly depend on the lipophilicity of the compds. and their ability to form the hydrogen bonds with the receptor. However, the binding sites in CCK-A receptor seem to be slightly rigid as compared to those in CCK-B or gastrin receptor. The latter two appear to have similar binding features.
IT 103373-61-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(quant. structure-activity relationship study on nonpeptidal cholecystokinin antagonists)
RN 103373-61-1 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1998:249001 CAPLUS Full-text
DN 128:292237
OREF 128:57827a,57830a
TI Synthesis and evaluation of 11C-labeled nonpeptide antagonists for cholecystokinin receptors: [11C]L-365,260 and [11C]L-365,346
AU Haradahira, Terushi; Inoue, Osamu; Kobayashi, Kaoru; Suzuki, Kazutoshi
CS Natl. Inst. Radiol. Sci., Chiba, 263, Japan
SO Nuclear Medicine and Biology (1998), 25(3), 203-208
CODEN: NMBIEO; ISSN: 0969-8051
PB Elsevier Science Inc.
DT Journal
LA English
AB 11C-labeled cholecystokinin (CCK) receptor antagonists, 3R(+)-N-(2,3-dihydro-1-[11C]methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepine-3- yl)-N'-(3-methylphenyl)urea ([11C]L-365,260) and its (S)-enantiomer ([11C]L-365,346), have been synthesized and evaluated in vivo for use in CCK receptor studies with positron emission tomog. (PET). Selective N-methylation of a racemic precursor with [11C]iodomethane and subsequent optical resolution of the racemate with HPLC afforded optically pure [11C]L-365,260 and [11C]L-365,346, which are selective for CCK-B (central-type) receptors and CCK-A (peripheral-type) receptors, resp. Biodistribution studies in mice showed very low brain uptakes (<0.8% dose/g) of the radioactivities after i.v. injections of these compds., although that of brain CCK-B receptor-selective [11C]L365,260 was 2-fold that of [11C]L-365,346. In peripheral organs, uptake of the radioactivity in the pancreas was the highest among the organs tested after the injection of [11C]L-365,346 and was 3-fold that of [11C]L-365,260. It was also observed that high uptake of [11C]L-365,346 in rat pancreas was significantly inhibited by a simultaneous injection with a large dose of L-365,346 (3 mg/kg). These preliminary results suggest that the nonpeptide CCK antagonist [11C]L-365,346 may be useful for probing pancreatic CCK-A receptors by PET. Owing to the very low brain permeability however, [11C]L-365,260 may have no potential as a PET tracer for probing brain CCK-B receptors.
IT 206115-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and evaluation of 11C-labeled nonpeptide antagonists for cholecystokinin receptors: [11C]L-365,260 and [11C]L-365,346)
RN 206115-23-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-methylphenyl)- (CA INDEX NAME)



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1995:998140 CAPLUS Full-text
DN 124:176161
OREF 124:32675a,32678a
TI Preparation of 1,4-benzodiazepin-2-one-1-acetamides as cholecystokinin-A receptor agonists
IN Aquino, Christopher Joseph; Dezube, Milana; Sugg, Elizabeth Ellen; Sherrill, Ronald George; Willson, Timothy Mark; Szewczyk, Jerzy Ryszard
PA Glaxo Wellcome Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9528399	A1	19951026	WO 1995-EP1335	19950413
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9524462	A	19951110	AU 1995-24462	19950413
	EP 755394	A1	19970129	EP 1995-918554	19950413
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09511998	T	19971202	JP 1995-526694	19950413
	ZA 9503111	A	19960123	ZA 1995-3111	19950418
	US 5795887	A	19980818	US 1996-718552	19961011
PRAI	GB 1994-7468	A	19940415		
	GB 1994-7499	A	19940415		
	GB 1994-20699	A	19941014		
	GB 1994-20702	A	19941014		
	WO 1995-EP1335	W	19950413		

OS MARPAT 124:176161
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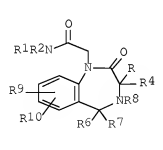
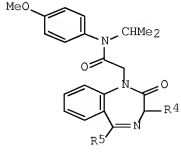


I



II

AB Title compds. [I; R = (CH2)n(NH)p(CO)q(NH)rR3; R1 = (cyclo)alkyl, (un)substituted Ph; R2 = (cyclo)alkyl, (un)substituted Ph, alkenyl, etc.; NR1R2 = tetrahydroquinolyl, substituted benzazepinyl; R3 = H, (cyclo)alkyl,

(un)substituted Ph, heteroaryl, etc.; R4 = H, alkyl, alkoxy, etc.; R6 = (CH2)mR5; R5 = H, = (cyclo)alkyl, (un)substituted Ph, -heteroaryl, etc.; R7 = H; R6R7 = O; R8 = H, (un)substituted alkyl, NH2, CO2H, etc.; R7R8 = bond; R9,R10 = H or halo; m,n = 0-3; p,q,r, = 0 or 1] were prepared Thus, 3-benzyloxycarbonylamino-5-(3-pyridyl)-1,3- dihydrobenzo[e][1,4]diazepin-2-one was N-alkylated by BrCH2CON(CHMe2)C6H4(OMe)-4 (preparation given) and the deprotected product condensed with PhNCO to give title compound II (R4 = NHCONHPh, R5 = 3-pyridyl). II (R4 = 1H-indazol-3-ylmethyl, R5 = 2-pyridyl)(preparation not given) gave 100% inhibition of guinea pig gall bladder segment contraction at 30μM in vitro and 2.5% rat gastric emptying at 0.1mol/kg i.p.

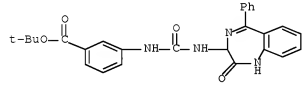
IT 173459-49-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 1,4-benzodiazepin-2-one-1-acetamides as cholecystokinin-A receptor agonists)

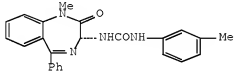
RN 173459-49-9 CAPLUS

CN Benzoic acid, 3-[[[(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)amino]carbonyl]amino]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

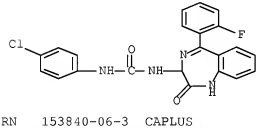
L5 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1994:217628 CAPLUS Full-text
DN 120:217628
OREF 120:38649a,38652a
TI Development of 1,4-benzodiazepine cholecystokinin type B antagonists
AU Bock, Mark G.; DiPardo, Robert M.; Evans, Ben E.; Rittle, Kenneth E.; Whitter, Willie L.; Garsky, Victor M.; Gilbert, Kevin F.; Leighton, James L.; Carson, Kenneth L.; et al.
CS Dep. Med., Merck Res. Lab., West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (1993), 36(26), 4276-92
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



I

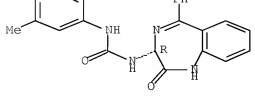
AB A series of 3-(arylureido)-5-phenyl-1,4-benzodiazepines, nonpeptidal antagonists of the peptide hormone cholecystokinin (CCK), are described. Derived by reasoned modification of the CCK-A selective 3-carboxamido-1,4-benzodiazepine, MK-329, the development of potent, orally effective compds. in which selectivity for the CCK-B receptor subtype was achieved. The principal lead structure that emerged from these studied is L-365,260 (I), a compound which has been submitted for clin. evaluation. Details of the ability to modulate the receptor interactions of these benzodiazepines by appropriate structure modifications are discussed which imply the possibility of further refining the CCK-B receptor affinity and selectivity of this class of compds.

IT 103373-61-1P 153840-06-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cholecystokinin type B antagonist activity of)
RN 103373-61-1 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)



RN 153840-06-3 CAPLUS
CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-methylphenyl)-, (R)- (9CI) (CA INDEX NAME)

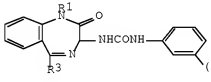
Absolute stereochemistry.



L5 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1993:580835 CAPLUS Full-text
DN 119:180835
OREF 119:32335a,32338a
TI (Phenylureido)benzodiazepinone antagonists of gastrin and/or cholecystokinin
IN Carr, Robin Arthur Ellis; Pass, Martin; Shah, Pritom
PA Glaxo Group Ltd., UK
SO Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 538945	A1	19930428	EP 1992-203188	19921019
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	WO 9308175	A1	19930429	WO 1992-EP2385	19921019
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9227596	A	19930521	AU 1992-27596	19921019
	CN 1074216	A	19930714	CN 1992-113397	19921023
	ZA 9208200	A	19930813	ZA 1992-8200	19921023
PRAI	GB 1991-22540	A	19911024		
	GB 1991-22551	A	19911024		
	GB 1991-22591	A	19911024		
	WO 1992-EP2385	A	19921019		

OS MARPAT 119:180835
GI



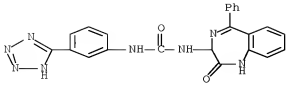
I

AB The title compds. I [R1 = CH2CONR4R5, XYR6, Ph, C3-7 cycloalkyl, (un)substituted alkyl; R4, R5 = H, Ph, C1-4 alkyl; NR4R5 = (un)substituted 5-7-membered heterocyclic ring; X = C1-3 (un)branched alkylene; Y = CO, C(OR9)2, C(SR9)2; R9 = C1-3 alkyl or 2R9 groups together may form a C2-4 alkylene chain; R6 = C1-6 alkyl, (un)substituted Ph, C3-7 cycloalkyl, adamantyl; R2 = NR7SO2CF3, SO2NR7COR8, CONR7SO2R8; R7 = H, C1-4 alkyl; R8 = C1-4 alkyl; R3 = (un)substituted Ph; n = 0, 1], useful for treating gastrin- or cholecystokinin-moderated diseases, are prepared and pharmaceutical formulations containing I are presented. Thus, 3-amino-2,3-dihydro-N-methyl-2-oxo-N,5-diphenyl-1H-1,4-benzodiazepine-1- acetamide was coupled with 3-(1H-tetrazol-5-yl)benzenamine hydrochloride, forming 2,3-dihydro-N-methyl-2-oxo-N,5-diphenyl-3-[[[3-(1H-tetrazol-5- yl)phenyl]amino]carbonyl]amino]-1H-1,4-benzodiazepine-1-acetamide (II). II demonstrated guinea pig cholecystokinin-B antagonist activity in an isolated ileum longitudinal muscle-myenteric plexus preparation of pKb 11.6.

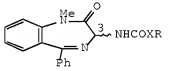
IT 150007-37-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antagonists of gastrin and/or cholecystokinin)

RN 150007-37-7 CAPLUS

CN Urea, N-(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-[3-(2H-tetrazol-5-yl)phenyl]- (CA INDEX NAME)


Ph
N
N
N
H
NH
C
O
NH
N
N
H
O

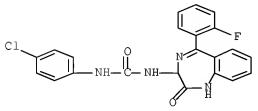
L5 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1992:604536 CAPLUS Full-text
DN 117:204536
OREF 117:35068h,35069a
TI Design of cholecystokinin peptidomimetics
AU Bock, Mark G.; DiPardo, Robert M.; Evans, Ben E.; Rittle, Kenneth E.; Veber, Daniel F.; Whitter, Willie L.; Chang, Raymond S. L.; Lotti, Victor J.; Anderson, Paul S.; Freidinger, Roger M.
CS Dep. Med. Chem., Merck Sharp and Dohme Res. Lab., West Point, PA, USA
SO Journal of Controlled Release (1992), 21(1-3), 73-80
CODEN: JCREEC; ISSN: 0168-3659
DT Journal
LA English
GI



I, R=2-indolyl, X=bond, 3S
II, R=3-methylphenyl, X=NH, 3R

AB Cholecystokinin (CCK) is a polypeptide hormone which occurs in numerous mol. forms at various sites throughout the peripheral and central nervous systems. The wide range of physiol. responses which have been attributed to CCK has stimulated the search for agents which mimic or block its action. Two principal CCK receptor subtypes have been characterized and numerous peptide substrate analogs have been identified which bind potently with these receptor subtypes. However, a number of insufficiencies inherent in peptide structures have limited their application as drugs. These shortcomings include rapid breakdown to inactive substances by proteases, poor transport, and rapid excretion. Such properties limit the duration of action and bioavailability of peptides and have prompted researchers to initiate the development of compds. which have less peptide character, indeed, to develop total nonpeptidal agents. We describe the discovery of several potent non-peptide CCK antagonists which display selectivity vs. the peripheral (CCK-A) and central (CCK-B) receptors. The most thoroughly characterized of these agents are the benzodiazepine derivs. MK-329 (I) and L-365260 (II). The novel CCK antagonists are orally effective, long acting and devoid of agonist activity. I and II should find widespread use in delineating the function of CCK receptors in human physiol. and may have potential clin. application.

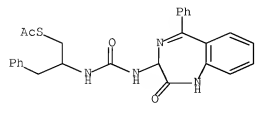
IT 103373-61-1
RL: BIOL (Biological study)
(cholecystokinin antagonist, design and activity of)
RN 103373-61-1 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)



L5 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1992:235102 CAPLUS Full-text
DN 116:235102
OREF 116:39805a,39808a
TI Preparation of N-(mercaptoalkyl)ureas as enkephalinase inhibitors
IN Clemence, Francois; Le Martret, Odile; Petit, Francis
PA Roussel-UCLAF, Fr.
SO Eur. Pat. Appl., 74 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 465369	A1	19920108	EP 1991-401858	19910704
	EP 465369	B1	19940413		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FR 2664269	A1	19920110	FR 1990-8539	19900705
	FR 2664269	B1	19921002		
	CA 2046264	A1	19920106	CA 1991-2046264	19910704
	JP 04230358	A	19920819	JP 1991-189598	19910704
	AT 104278	T	19940415	AT 1991-401858	19910704
	ES 2063465	T3	19950101	ES 1991-401858	19910704
	US 5190974	A	19930302	US 1991-725985	19910705
	US 5674864	A	19971007	US 1995-449290	19950524
PRAI	FR 1990-8539	A	19900705		
	EP 1991-401858	A	19910704		
	US 1991-725985	A3	19910705		
	US 1992-970117	A3	19921102		

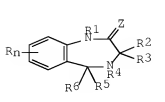
OS MARPAT 116:235102
AB R1SCH2CH(AR2)NHC(:X)(CH2)nNR3R4[A = (hydroxy- or alkoxy-substituted) alkylene or -alkenylene; R1 = H, R5CO; R2 = (hetero)cyclic radical; R3,R4 = H, OH, alkoxy, acyl, CO2H, alkyl, etc.; NR3R4 = heterocyclyl; R5 = (cyclo)alkyl, alkenyl, heterocyclyl, (substituted)amino, etc.; X = O, S; n = 0-4] were prepared Thus, AcSCH2CH(CH2Ph)NH2.HCl (preparation from phenylalanine given) was treated with ClCO2CCl3 and the isocyanate product condensed with MeNHOH to give, after hydrazinolysis, HSCH2CH(CH2Ph)NHCONR3R4 (II; R3 = OH, R4 = Me). II (R3 = R4 = Pr) had ED50 of 33 mg/kg orally against HOAc-induced writhing in mice.
IT 141402-97-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as enkephalinase inhibitor)
RN 141402-97-3 CAPLUS
CN Ethanethioic acid, S-[2-[[[(2,3-dihydro-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)amino]carbonyl]amino]-3-phenylpropyl] ester (CA INDEX NAME)



L5 ANSWER 19 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1989:497296 CAPLUS Full-text
Correction of: 1987:67359
DN 111:97296
Correction of: 106:67359
OREF 111:16377a,16380a
TI Benzodiazepine derivatives and their pharmaceutical use
IN Freidinger, Roger M.; Bock, Mark G.; Evans, Ben E.
PA Merck and Co., Inc., USA
SO Eur. Pat. Appl., 290 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 167919	A2	19860115	EP 1985-107842	19850625
	EP 167919	A3	19861105		
	EP 167919	B1	19930505		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	CA 1332410	C	19941011	CA 1985-484488	19850619
	NO 8502558	A	19851227	NO 1985-2558	19850625
	NO 173651	B	19931004		
	NO 173651	C	19940112		
	AU 8544152	A	19860102	AU 1985-44152	19850625
	DK 8502872	A	19860225	DK 1985-2872	19850625
	DK 175264	B1	20040802		
	AT 88998	T	19930515	AT 1985-107842	19850625
	ZA 8504764	A	19860226	ZA 1985-4764	19850626
	JP 61063666	A	19860401	JP 1985-138064	19850626
	US 5004741	A	19910402	US 1988-269212	19881109
	AU 8944563	A	19900405	AU 1989-44563	19891110
	AU 640113	B2	19930819		
	AU 9211171	A	19920514	AU 1992-11171	19920221
	AU 9471615	A	19941222	AU 1994-71615	19940831
	AU 679085	B2	19970619		
PRAI	US 1984-624854	A	19840626		
	US 1985-705272	A	19850225		
	US 1985-741972	A	19850610		
	EP 1985-107842	A	19850625		
	US 1987-26420	A3	19870316		

OS MARPAT 111:97296
GI



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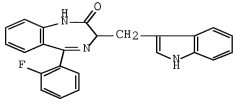


II

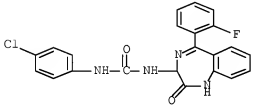
AB 1,4-Benzodiazepines I [n = 1,2; R = H, NO2, CF3, cyano, etc.; R1 = alkyl, alkenyl, carboxyalkyl, aminoalkyl, etc.; Z = O, S, H2, NH, etc.; R2, R6 = H, OH, Me; R3 = substituted alkyl; R4 = H, alkyl, acyl, etc.; R5 = H, alkyl, (un)substituted Ph, etc.], which are cholecystokinin (CCK) inhibitors, were prepared 2-Amino-2'-fluorobenzophenone was treated with tryptophan acid chloride-HCl and NaOH to give benzodiazepinone (R)-II. (R)-II inhibited CCK binding in isolated rat pancreas with an IC50 of o.40 μM.

IT 103373-61-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholecystokinin inhibitor)

RN 103373-61-1 CAPLUS

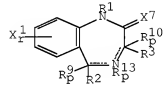
CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)



L5 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1989:135272 CAPLUS Full-text
DN 110:135272
OREF 110:22339a,22342a
TI Preparation of benzodiazepines as cholecystokinin and gastrin inhibitors
IN Evans, Ben E.; Freidinger, Roger M.; Bock, Mark G.
PA Merck and Co., Inc., USA
SO Eur. Pat. Appl., 254 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 284256	A1	19880928	EP 1988-302141	19880311
	EP 284256	B1	19940601		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 4820834	A	19890411	US 1987-26420	19870316
	IL 85668	A	19950330	IL 1988-85668	19880308
	AT 106401	T	19940615	AT 1988-302141	19880311
	ES 2052704	T3	19940716	ES 1988-302141	19880311
	AU 8813133	A	19880915	AU 1988-13133	19880315
	DK 8801395	A	19890106	DK 1988-1395	19880315
	DK 175575	B1	20041213		
	CA 1332411	C	19941011	CA 1988-561493	19880315
	JP 63238069	A	19881004	JP 1988-60643	19880316
	JP 3039783	B2	20000508		
	ZA 8801866	A	19881026	ZA 1988-1866	19880316
	US 5004741	A	19910402	US 1988-269212	19881109
	AU 9211171	A	19920514	AU 1992-11171	19920221
	AU 9471615	A	19941222	AU 1994-71615	19940831
	AU 679085	B2	19970619		
PRAI	US 1987-26420	A	19870316		
	US 1984-624854	A2	19840626		
	US 1985-705272	A2	19850225		
	US 1985-741972	A2	19850610		
	EP 1988-302141	A	19880311		

OS CASREACT 110:135272; MARPAT 110:135272
GI



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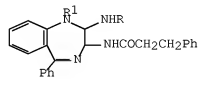
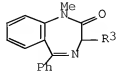


II



III

AB The title compds. [I; R1 = H, alkenyl, (un)substituted alkyl, etc.; R2 = H, alkyl, pyridyl, (un)substituted Ph, etc.; R3 = X11NR18(CH2)qR16, X11NR18COX11R7, NH(CH2)2-3NHR7, NH(CH2)2-3NHCOR7, etc.; R7 = naphthyl, (un)substituted Ph, heterocyclyl, etc.; R9, R10 = H, OH, Me; R13 = H, alkyl, acyl, O, cycloalkyl; R16 = naphthyl, 2-indolyl; R18 = H, alkyl; X1 = H, NO2, CF3, OH, alkyl, etc.; X7 = O, S, H2, etc.; X11 = bond, alkylidene (sic); p = 0, 1; q = 0-4; r = 1, 2], useful as cholecystokinin and gastrin receptor binding inhibitors, were prepared 3-Amino-1,3-dihydro-5-phenyl-2H-1,4-

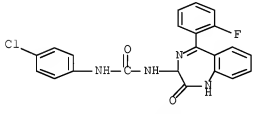
benzodiazepine-2-one was stirred with L-PhCH2CH(CO2H)NHCO2CMe3 in DMF containing EtN:C:N(CH2)3NMe2 and 1-hydroxybenzotriazole to give diaminobenzodiazepine II (R = CO2CMe3, R1 = H) which was stirred 30 min with NaH in DMF followed by stirring 1 h with MeI to give II (R = CO2CMe3, R1 = Me). The latter was stirred with HCl in EtOAc followed by flash chromatog. on silica gel to give sep., (3R)- and (3S)-II (R = H, R1 = Me) the latter of which was treated successively with PhNCS and CF3CO2H to give aminobenzodiazepineone (3S)-III (R3 = NH2). The latter was stirred 30 min with 2-indolecarbonyl chloride in CH2Cl2 containing Et3N to give (3S)-III [R3 = (2-indolylcarbonyl)amino] which had IC50 of 0.0008 and 0.17 μM for cholecystokinin and gastrin binding in vitro, resp.

IT 103373-61-1P 119506-69-3P 119506-75-1P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholecystokinin and/or gastrin inhibitor)

RN 103373-61-1 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)



RN 119506-69-3 CAPLUS

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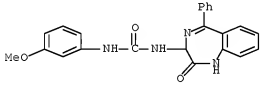
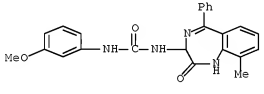
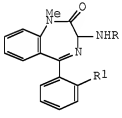


RN 119506-75-1 CAPLUS

CN Urea, N-(2,3-dihydro-9-methyl-2-oxo-5-phenyl-1H-1,4-benzodiazepin-3-yl)-N'-(3-methoxyphenyl)- (CA INDEX NAME)

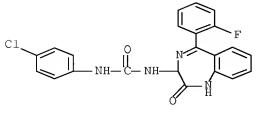


L5 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1989:38961 CAPLUS Full-text
DN 110:38961
OREF 110:6495a,6498a
TI Benzodiazepine gastrin and brain cholecystokinin receptor ligands; L-365,260
AU Bock, Mark G.; DiPardo, Robert M.; Evans, Ben E.; Rittle, Kenneth E.; Whitter, Willie L.; Veber, Daniel F.; Anderson, Paul S.; Freidinger, Roger M.
CS Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SO Journal of Medicinal Chemistry (1989), 32(1), 13-16
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 110:38961
GI



I

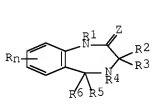
AB A novel series of 3-substituted 1,4-benzodiazepine, e.g., (R,S)-, (R)-, or (S)-I (R = 4-ClC6H4CO, R1 = F; R = 4-ClC6H4NHCO, 3-MeC6H4NHCO, R1 = H) were prepared as ligands for the receptors of the peptide hormones gastrin and cholecystokinin. E.g., I (R = H, R1 = H) was treated with 3-MeC6H4NCO to give I (R = 3-MeC6H4NHCO, R1 = H). These compds., which have high specificity and display nanomolar binding affinity for the gastrin and brain cholecystokinin receptors, represent the first examples of nonpeptidal substances with such a selectivity profile. L-365,260 (R)-I (R = 4-MeC6H4NHCO, R1 = H) shows IC50 values of 1.1 nM and 2.0 nM for the gastrin and brain cholecystokinin receptors, resp. The structural features which distinguish these gastrin and centrally selective cholecystokinin ligands from peripheral cholecystokinin antagonists are discussed.
IT 103373-61-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and binding of, with gastrin and brain cholecystokinin receptors)
RN 103373-61-1 CAPLUS
CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)

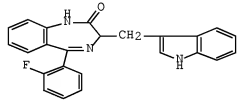


L5 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1987:67359 CAPLUS Full-text
DN 106:67359
OREF 106:11083a,11086a
TI Benzodiazepine derivatives and their pharmaceutical use
IN Freidinger, Roger M.; Bock, Mark G.; Evans, Ben E.
PA Merck and Co., Inc. , USA
SO Eur. Pat. Appl., 290 pp.
CODEN: EPXXDW
DT Patent
LA English

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 167919 A2		19860115	EP 1985-107842	19850625
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
PRAI US 1984-624854		19840626		
US 1985-705272		19850225		
US 1985-741972		19850610		

GI


I


II

AB 1,4-Benzodiazepines I [n = 1,2; R = H, NO2, CF3, cyano, etc.; R1 = alkyl, alkenyl, carboxyalkyl, aminoalkyl, etc.; Z = O, S, H2, NH, etc.; R2 and R6 are H, OH, Me; R3 = substituted alkyl; R4 = H, alkyl, acyl, etc.; R5 = H, alkyl, (un)substituted Ph, etc.], which inhibited cholecystokinin, were prepared 2-Aminophenyl 2-fluorophenyl ketone was teated with tryptophan and chloride hydrochloride and NaOH to give benzodiazepinone derivative II.

IT 103373-61-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as cholecystokinin inhibitor)

RN 103373-61-1 CAPLUS

CN Urea, N-(4-chlorophenyl)-N'-[5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1H-1,4-benzodiazepin-3-yl]- (CA INDEX NAME)

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=> d l2; d his; log y
L2 HAS NO ANSWERS
L1              STR
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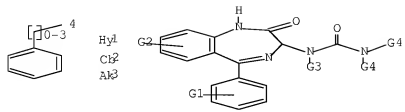


```
 G1 C,H,O,S
 G2 H,Me,Et,n-Pr,i-Pr,X
 G3 H,Me,Et,n-Pr,i-Pr
 G4 H,[@1],[@2],[@3],[@4]


Structure attributes must be viewed using STN Express query preparation.
L2              QUE  ABB=ON  PLU=ON  L1



     (FILE 'REGISTRY' ENTERED AT 18:22:34 ON 14 APR 2009)
                DEL HIS Y
L1              STRUCTURE UPLOADED
L2              QUE L1
L3            3 S L2
L4           51 S L2 FUL

     FILE 'CAPLUS' ENTERED AT 18:24:00 ON 14 APR 2009
L5           22 S L4

COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               125.08     311.66

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                               -18.04     -18.04

STN INTERNATIONAL LOGOFF AT 18:25:17 ON 14 APR 2009
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